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Adaptation of Oriented and Unoriented Color-Selective Neurons in Human Visual Areas

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Summary

Primary visual cortex contains at least two distinct populations of color-selective cells: neurons in one have circularly symmetric receptive fields and respond best to reddish and greenish light, while neurons in another have oriented receptive fields and a variety of color preferences. The relative prevalence and perceptual roles of the two kinds of neurons remain controversial, however. We used fMRI and a selective adaptation technique to measure responses attributable to these two populations. The technique revealed evidence of adaptation in both populations and indicated that they each produced strong signals in V1 and other human visual areas. The activity of both sets of neurons was also reflected in color appearance measurements made with the same stimuli. Thus, both oriented and unoriented color-selective cells in V1 are important components of the neural pathways that underlie perception of color.

Introduction

As a first step toward understanding the cortical basis of color vision, researchers classified cells by the selectivity of their responses to various colored patterns (e.g., Livingstone and Hubel, 1984; Thorell et al., 1984). For example, classically labeled red-green cells generally respond well to patterns that stimulate the long-wavelength (L) and medium-wavelength (M) cones in opposition, as would a spot of reddish light that excited the L cones more than, and the M cones less than, a gray background. Such cells respond poorly to patterns that stimulate the L and M cones in the same direction relative to the background, as would a spot of white light. Classically labeled light-dark (or luminance) cells, on the other hand, respond well to the white spot and poorly to the reddish spot. Classical blue-yellow cells respond well to short-wavelength cone stimulation in opposition to L and M cone stimulation. Other color-selective cells prefer "noncardinal", color directions and so fall in between these three categories. One such neuron might prefer, for example, L cone stimulation in opposition to M cone stimulation that is half as strong.

One particularly contentious issue concerns the orientation selectivity of color-selective neurons. While there is general agreement that most cells in V1 that prefer light-dark are also orientation selective, the number of oriented cells preferring other colors has been under dispute (Conway, 2001; De Valois et al., 2000; Friedman et al., 2003; Johnson et al., 2001, 2004; Landisman and Ts'o, 2002a, 2002b; Lennie et al., 1990; Leventhal et al., 1995; Livingstone and Hubel, 1984; Thorell et al., 1984). Recent reviews of the literature suggest that, although their interpretations differ, all studies that have recorded widely from V1 have found oriented cells that prefer colors other than luminance (Gegenfurtner, 2003; Schluppeck and Engel, 2002). Johnson and colleagues (2001, 2004) made the most detailed measurements of joint color and spatial tuning, and on the basis of these proposed that unoriented and oriented color-selective neurons comprise two separable populations in cortex.

The relative sizes of these two populations of neurons, however, remain controversial, as do their functions: specifically, it is unclear whether the oriented color-selective neurons in V1 are part of the critical pathway for color perception, or whether they simply provide input to pathways that are important for perception of form. We addressed these issues by measuring selectivity for color and orientation in human visual areas with functional MRI (fMRI) and comparing those results to perceptual measurements made with the same stimuli. We found evidence that both oriented and unoriented populations provide strong signals that are important for color perception.

We used an adaptation procedure originally described in the psychophysical literature (Bradley et al., 1988). In our experiment, subjects adapted to one of four high-contrast sinusoidal grating patterns. The patterns appeared either red-green or light-dark and were oriented either horizontally or vertically (see Figure 1 and Experimental Procedures). Using methods developed previously (Engel and Furmanski, 2001), we measured fMRI response to four lower-contrast test patterns before and after adaptation. The test patterns were also red-green or light-dark, and horizontal or vertical. Effects of adaptation were measured as reductions in responsiveness of cortical regions to the test patterns. In visual areas containing many oriented neurons that respond to red-green, for example, we expected red-green adaptation to produce large reductions in responses to red-green test patterns that were the same orientation as the adapting pattern and much smaller reductions in responses to all other patterns. In visual areas containing many unoriented neurons that respond to red-green, we expected red-green adaptation to produce large reductions in response to red-green test patterns at both orientations and smaller reductions in response to light-dark test patterns.

Results

Subjects viewed low-contrast test patterns either presented alone (no adaptation scans; Figure 1) or following a high-contrast adaptor (adaptation scans). Test patterns presented in the no adaptation scans alternated with a gray mean field. The tests thus repre-

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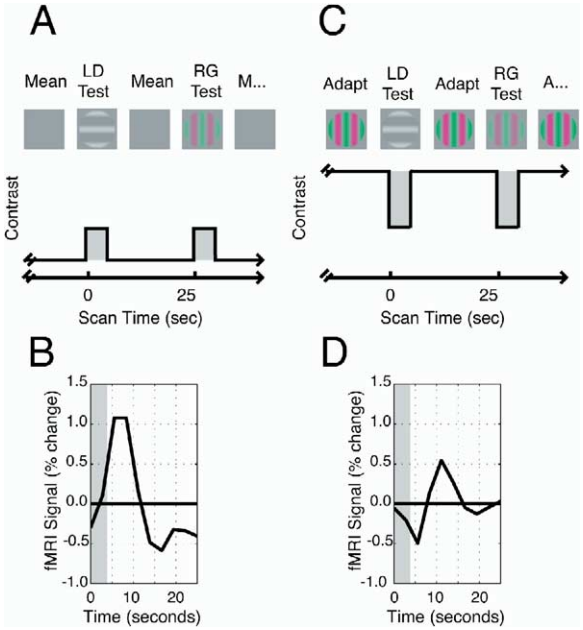

Figure 1. Experimental Methods

(A) In the no adaptation scans, 4 s low-contrast test stimuli alternated with 21 s mean gray field presentations.

(B) Grand average response of V1 to test stimuli in the no adaptation scans. Tests generated positive peaks in the fMRI time course, whose amplitude reflected the strength of the test. Shaded areas mark stimulus presentations.

(C) In adaptation scans, the same low-contrast test stimuli alternated with high-contrast adaptors. Adaptation scans were preceded by 1 min presentations of the adaptor.

(D) Grand average response of V1 to test stimuli in adaptation scans. Tests generated negative peaks in the fMRI time course, whose depth reflected the strength of the test. The reappearance of the adaptor also generated a positive "rebound" peak. In all time series plots, the y axis zero point, or baseline response, was set to the average of the time series.

sented increases in contrast, which produced increases in neural activity and so generated positive peaks in the fMRI time course (see Figure 1). Test stimuli presented during adaptation scans alternated with high-contrast adaptors. Because the test stimuli were lower contrast than the adaptors, they often generated negative peaks in the fMRI time course as activity fell from the high levels produced by the high-contrast adaptors. The depth of the negative peaks reflected the strength of response to the tests, with deeper peaks corresponding to weaker responses. Additionally, in some cases the test stimuli produced small positive peaks even in the adaptation scans, presumably because the response to the adaptor had fallen due to self-adaptation (see below).

Selective effects of adaptation were visible in our data as differences in the magnitudes of test responses during the adaptation scans. Test contrasts were carefully chosen to produce equal responses in cortex during the no adaptation scans, allowing differences observed during the adaptation scan to be attributed to effects of the adaptor. For example, in an adaptation scan, deeper negative peaks in response to red-green vertical tests than to the other tests indicated that the adaptor reduced red-green vertical responses relative to the other responses. Thus, negative response peaks per se were not indicative of adaptation, but differences in depths of the peaks were. Note further that this design and logic made unobservable general adaptation that affected equally all test stimuli.

In both no adaptation and adaptation scans, the amplitude of cortical response to the test was estimated by fitting gamma functions to the peaks that coincided with the test presentation, either positive or negative. Mean amplitudes were computed across subjects and are plotted with across-subject standard errors in Figures 2 and 3. The time courses also often showed a secondary, later peak corresponding to the reappearance of the adaptor following the test. These secondary peaks had minimal effect on the accuracy of our response amplitude estimates, as can be seen by comparing the amplitude estimates relative to the height of the initial peaks in the time courses in Figures 2 and 3.

Adaptation Jointly Selective for Color and Orientation

In almost all visual areas, adaptation produced effects that were jointly selective for color and orientation. Data from V1 averaged across adaptation colors are shown in Figure 2 (left). Stimuli presented prior to adaptation generated positive and roughly equal peaks for all tests. Following adaptation, presenting the test that was the same color and orientation as the adaptor generated a large negative peak, indicative of a very weak neural response. The response to these tests was indistinguishable from the response to a zero contrast test presentation, indicating that adaptation nearly abolished stimulus-related activity in V1. Presentations of patterns that differed in either orientation or color from the adaptor produced much smaller negative peaks, indicative of a much stronger neural response.

Jointly selective effects of adaptation were also visible when examining each adaptor color separately. An example is shown in the middle and right panels of Figure 2, which plot V1 responses for the two adaptation conditions. For red-green adaptation, the red-green test at the same orientation as the adaptor produced the weakest response, while for light-dark adaptation the light-dark test at the same orientation as the adaptor produced the weakest response. Similar results were seen in all later visual areas (Figure 3; visual areas were defined using retinotopic organization [see Experimental Procedures]; we could not segregate regions V3, V3a, and V7 and so label the combined region V3m).

Adaptation Selective for Color or Orientation

For red-green adaptors, some adaptation transferred to the red-green test pattern that differed in orientation from the adaptor. In V1, for example, the red-green test that differed in orientation from the adaptor produced a relatively weak response that was visible as a shallow trough in the fMRI time course. While the response was not as weak as that to the red-green test at the same orientation as the adaptor, it was weaker than the response to light-dark stimulation at the same orientation. Hence, some of the effects of adaptation to red-

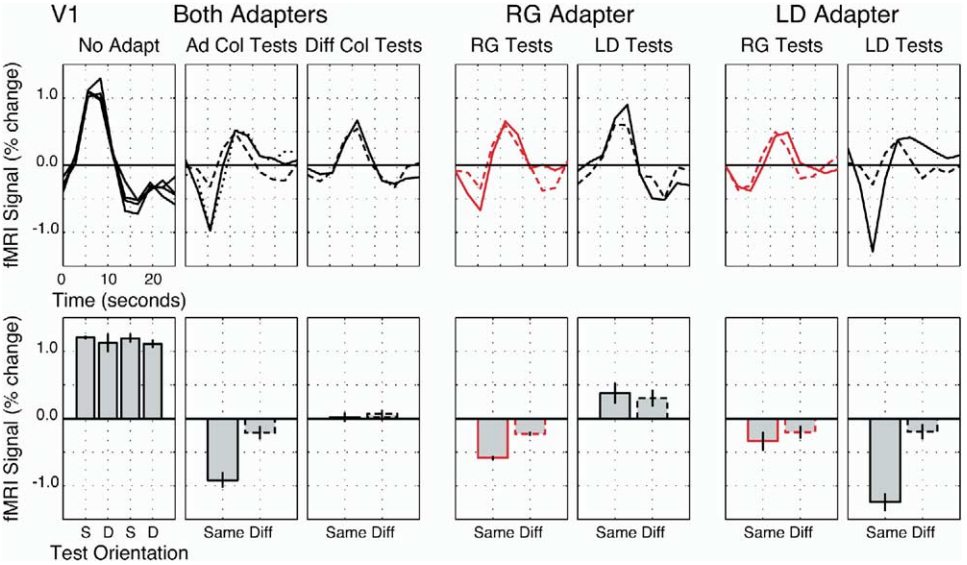

Figure 2. V1 Responses

Top panels show average time courses from V1, computed across four subjects, in response to the test stimuli. Solid lines plot responses to stimuli that were the same orientation as the adaptor; dashed lines plot responses to stimuli that differed in orientation from the adaptor. The dotted line plots the response to the zero contrast tests. Bottom panels show estimated amplitudes of responses, and error bars plot ±one standard error of the mean. Left panels show data averaged across adaptor color; middle and right panels show data averaged separately for red-green and light-dark adaptors. For the middle and right panels, color represents the color of the test (red for red-green, black for light-dark). In all cases, the response to the test that was the same orientation and color as the adaptor was reliably weaker than the responses to tests that differed in either orientation or color from the adaptor.

green were selective for color but not orientation. This component stands in addition to the jointly selective adaptation discussed above. Similar patterns for red-green adaptors were seen in other areas. This color-selective adaptation—transfer of adaptation to the stimulus that was the same color as but differed in orientation from the adaptor—was not seen for light-dark adaptors.

In areas V2 and V3m, adaptation to light-dark transferred to the red-green test that was the same orientation as the adaptor. Specifically, the red-green test at the same orientation as the light-dark adaptor produced a relatively weak response that was weaker than the red-green response that differed in orientation from the adaptor. This component of adaptation was selective for orientation but not color. Similar effects were not seen for red-green adaptors.

Overall, the response to the unadapted color was weaker for light-dark adaptors than for red-green ones. This simply reflects the fact that the light-dark adaptor produced a higher baseline level of activity in cortex than did the red-green adaptor; the higher baseline caused activity to drop further upon presentation of the low-contrast test stimuli. All our comparisons of interest involved comparing responses within an adaptor type and so are unaffected by baseline differences.

Modeling Population Responses

The simple examination of the conditional time courses that was performed above identified stronger effects of adaptation for stimuli that matched both the color and orientation of the adaptor than for other stimuli. One explanation of these effects is the presence of adaptation that is truly selective for color and orientation. An alternative explanation, however, is the combined presence of adaptation that transfers across orientation and adaptation that transfers across color; if just these two effects alone were present, and they combined in some way, then one would also expect the test that matched both the color and orientation of the adaptor to have the weakest response. Thus, to identify jointly selective adaptation its effects must be shown to be above and beyond the combined effects of color-specific and orientation-specific adaptation.

The analysis of variance (ANOVA) is the standard statistical tool to measure whether a joint effect is greater than the sum of two more general effects. ANOVA uses a simple linear model that estimates both general effects and a joint effect, usually called an interaction term. We fit this model to our data, primarily to test for the presence of joint effects. It also allowed coarse comparison between the sizes of general and joint effects, though such comparisons should be made with care, as discussed below.

Fitting the ANOVA model to our paradigm produced an equation with parameters that estimated four components of adaptation:

$$R(x_{col},x_{ori}) = u - Ad_{col}\,x_{col} - Ad_{ori}\,x_{ori} - Ad_{colori}\,x_{col}\,x_{ori} \quad (1)$$

where R is the amplitude of response to a test pattern, and u is the amplitude of the response were it unaffected by any of the subsequent adaptation terms. Ad_{col} is a

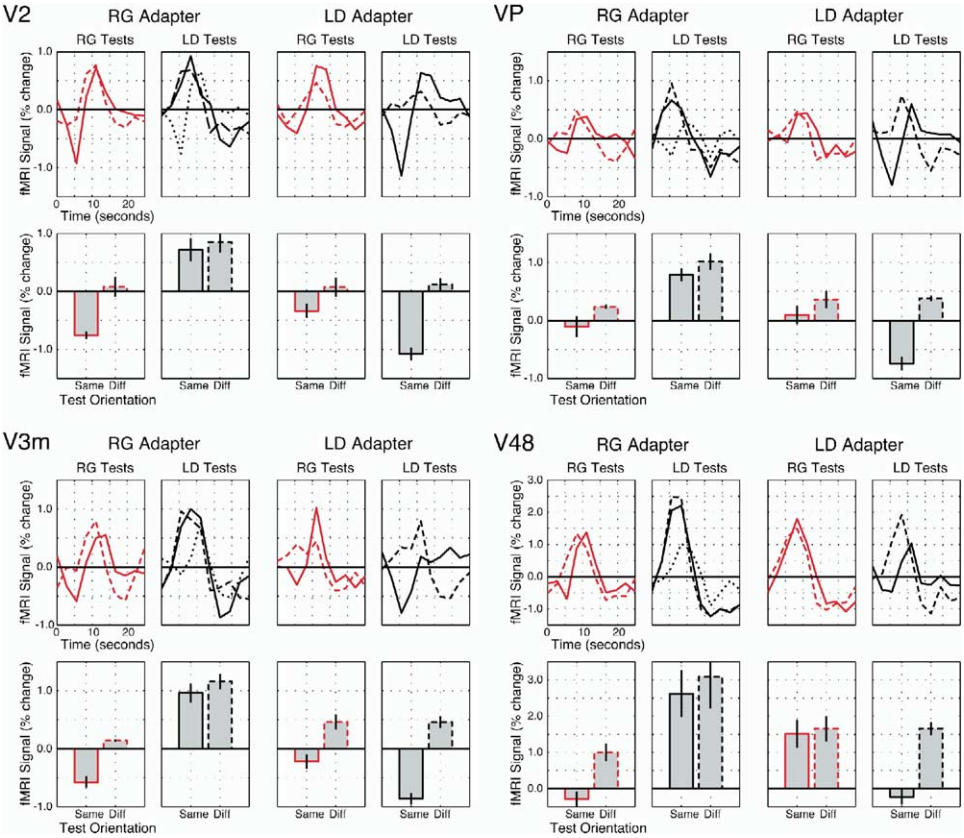

Figure 3. Extrastriate Responses

Panels are for visual areas V2, V3m, VP, and V4/8. Plotting conventions are as in Figure 2.

parameter that measures color-selective adaptation, i.e., effects of the adaptor that transfer to all stimuli of a given color, regardless of orientation. Similarly, Ad_{ori} is a parameter that measures orientation-selective adaptation, effects of the adaptor that transfer to all stimuli of a given orientation, regardless of color. Ad_{colori} measures adaptation that is jointly color- and orientation-selective; these are effects of adaptation on the test that is the same color and orientation as the adaptor that cannot be explained by adaptation that transfers across color and/or orientation. x_{col} and x_{ori} are condition codes used to allow the equation to predict the responses to all four tests; x_{col} was set to 1 if the test had the same color as the adaptor and 0 otherwise, and x_{ori} was set to 1 if the test had the same orientation as the adaptor and 0 otherwise.

The model has four unknowns and was fit to the responses to the four test patterns presented in each adaptation condition. Solving the system of four equations for each parameter yielded the following equations:

$$u = R(0,0) \quad (2)$$

$$Ad_{col} = R(0,0) - R(1,0) \quad (3)$$

$$Ad_{ori} = R(0,0) - R(0,1) \quad (4)$$

$$Ad_{colori} = (R(1,0) - R(1,1)) - (R(0,0) - R(0,1)) \quad (5)$$

Thus, the unadapted response, u, was estimated as the response to the test that differed from the adaptor in both color and orientation. Note that this term captures all effects other than the color-selective, orientation-selective, and jointly selective adaptation. Specifically, the unadapted response may be affected by general adaptation that transfers to all of the test stimuli; such general adaptation cannot be identified in this paradigm. The amount of color-selective adaptation was estimated as the reduction in response from unadapted levels that was produced by the test that was the same color as but differed in orientation from the adaptor. Similarly, the amount of orientation-selective adaptation was estimated as the reduction in response from unadapted levels produced by the test that was the same orientation as but differed in color from the adaptor. Finally, the amount of adaptation that was jointly color- and orientation-selective was estimated as the extra reduction in response produced when the test had the same color and orientation as the adaptor as compared to when the test had only the same orientation as the adaptor. Equation 5 can be rewritten as follows:

$$Ad_{colori} = (R(0,0) - R(1,1)) - ((R(0,0) - R(1,0)) + (R(0,0) - R(0,1))) \quad (6)$$

$$= (R(0,0) - R(1,1)) - (Ad_{col} + Ad_{ori}) \quad (7)$$

which makes it clear that the joint adaptation is esti-

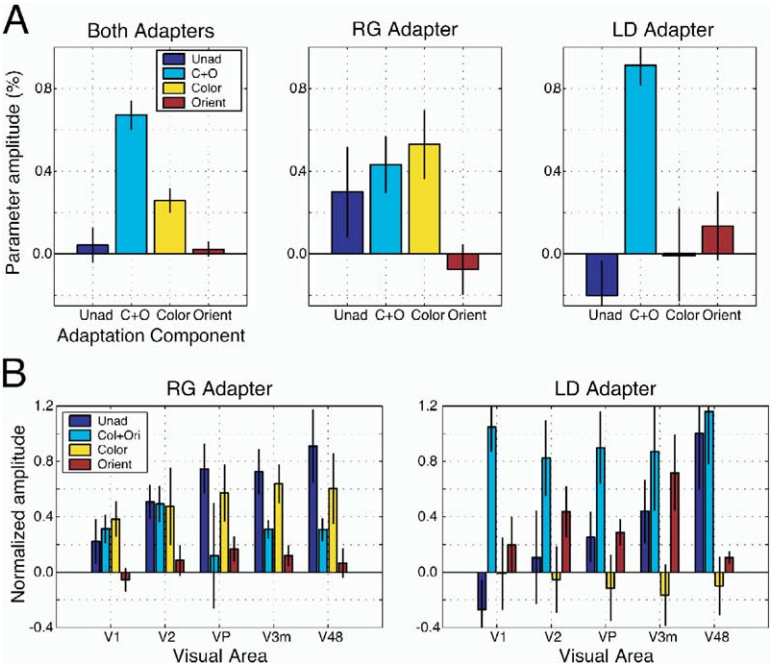

Figure 4. Quantified Effects of Adaptation

(A) Estimated parameters from area V1. Bars plot the mean ± one standard error of the parameters estimating the unadapted response, adaptation that is jointly selective for color and orientation, adaptation that is selective for color but generalizes across orientation, and adaptation that is selective for orientation and generalizes across color. See text for estimation procedures.

(B) Normalized parameter estimates from all visual areas. Parameters have been normalized by mean responses in the unadapted scans. Adaptation to red-green produced both jointly selective and color-selective effects in almost all visual areas. Adaptation to light-dark produced mainly jointly selective effects along with some orientation-selective effects.

mated as the reduction in response produced by the test that was the same color and orientation as the adaptor that was above and beyond the sum of the effects of color-selective and orientation-selective adaptation.

Reliability and Magnitude of Neural and Behavioral Adaptation Effects

We used the model to estimate the components of adaptation for each visual area in each subject. Figure 4A plots the mean parameters estimated from the V1 data. Figure 4B plots the mean parameters estimated from all visual areas. The parameters have been normalized to account for differences in overall fMRI response strength that arise between subjects and visual areas. We used the mean responses in the unadapted scans as a measure of overall response strength and normalized the parameters by dividing by them. Statistics reported below were performed on the normalized data, though similar results were obtained using raw scores.

Adaptation to red-green produced adaptation that was jointly selective for color and orientation in all visual areas (Figure 4, light blue bars; V1, $t = 3.1$; V2, $t = 3.8$; V3m, $t = 4.6$; and V4/8, $t = 3.8$; all reported tests have 3 d.f. where the t value for $p < 0.05$ is 2.35) except area VP, which showed relatively inconsistent and nonselective results. Adaptation to red-green also produced reliable color-specific adaptation that transferred to the red-green test pattern that differed in orientation from the adaptor (yellow bars; V1, $t = 3.01$; VP, $t = 2.79$; V3m, $t = 4.5$; V48, $t = 2.37$), though such trends were not highly reliable in V2. The jointly selective and the color-selective effects were of roughly equal magnitude, though there were nonsignificant trends for larger color-selective effects in most visual areas.

Adaptation to light-dark showed a different pattern of results. While it also produced adaptation that was jointly selective for color and orientation in all visual areas (V1, $t = 5.90$; V2, $t = 3.00$; VP, $t = 3.44$; V3m, $t = 2.03$; V48, $t = 3.03$), it did not produce any color-selective adaptation. In addition, adaptation to light-dark produced orientation-selective adaptation that transferred to the red-green test pattern that was the same orientation as the adaptor (Figure 4, red bars). This effect was large and reliable in areas V2 ($t = 2.38$) and V3m ($t = 2.6$) and very small, but still reliable, in area V48 ($t = 2.40$).

One could reasonably question whether it is appropriate to use the ANOVA model on our data, because the model assumes that effects of adaptation add, which has not been verified empirically. We believe that the ANOVA model's use is acceptable. In almost every fitting of the model (i.e., for each region and adaptor) one of the general effects is not reliably different than zero. For red-green adaptation, the orientation-selective effect is always close to zero, and for light-dark adaptation the color-selective effect never deviates reliably from zero. Even highly nonlinear models (e.g., multiplicative ones) predict that when one of the general effects is zero, the combination of the two general effects will be equal to the one that is different than zero. This is the same prediction made by the additive model. Thus, for most of the cases here, the additive ANOVA model and nonlinear models of the combination of simple effects are not likely to differ. The estimate of joint adaptation is then a valid measure of the *presence* of adaptation that is above and beyond the combination of the simple effects.

It remains possible, however, that our numerical estimate of the *magnitude* of joint adaptation could include some nonlinear interactions between the one general effect that is present and the joint effect. Accordingly, the magnitude of the jointly selective component of

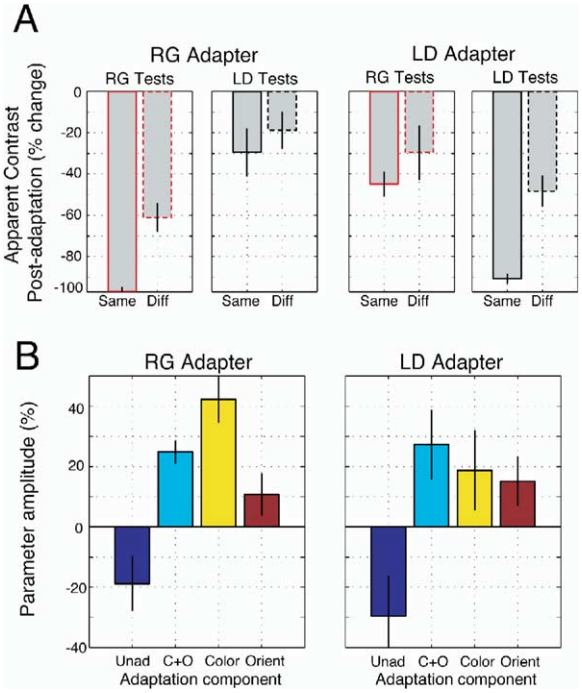

Figure 5. Behavioral Results

Subjects adjusted the contrast of unadapted stimuli to match the appearance of adapted ones. Test and adapting stimuli were the same as those used for the fMRI measurements. (A) The y axis shows the reduction in contrast, as a percentage of the original test contrast, that caused the unadapted test to match the appearance of the adapted test. Other plotting conventions are as in Figure 2. (B) Quantified effects of adaptation upon behavior. Parameters are as in Figure 4.

adaptation must be interpreted with care. One example of a nonlinear interaction is a floor effect. The present results may underestimate the joint effect, because neural responses to the test that is the same color and orientation as the adaptor are at some level beyond which responses can no longer be reduced. We are currently not aware of any models of adaptation that would give reason to believe that our analysis overestimates the jointly selective component of adaptation, but they remain a possibility. (Contrast response nonlinearities are one general concern but may be less important here because adaptation generally shifts neurons' contrast response functions horizontally along a log contrast axis [e.g., Ohzawa et al., 1985], and neural contrast response as measured with fMRI is a relatively linear function when plotted on a log contrast axis [e.g., Boynton et al., 1996].)

Behavioral adaptation for the same stimuli was measured using a contrast matching task, in which subjects adjusted the appearance of an unadapted stimulus to match the appearance of an adapted one (see Experimental Procedures). Behavioral adaptation showed most of the same effects that were found in the neural data (Figure 5). Adaptation to red-green showed joint selectivity ($t = 6.38$) as well as color selectivity ($t = 5.43$). Adaptation to light-dark was also jointly selective for color and orientation ($t = 2.34$).

Strength of Adaptation across Visual Areas

In later visual areas, the low-contrast test presentations generated positive peaks in the fMRI time course, even during the adaptation scans. In V4/8, for example (Figure 3), all tests except for the test of the same color and orientation as the adaptor generated positive peaks, which indicates that the low-contrast test generated more neural activity than the high-contrast adaptor. VP and V3m showed similar patterns. This effect was not small; in area V4/8, for example, a light-dark test grating of 8.6% contrast that was orthogonal to the adaptor produced a greater response than the 37.7% contrast light-dark adapting grating. The estimated unadapted responses (Figure 4, blue bars) show the strength of response to the low-contrast test that differed in color and orientation from the adaptor. The strength of this response is clearly larger in later visual areas.

The cause of these positive peaks was a relatively low baseline of activity provided by the adapting stimulus. The negative peaks produced by the zero contrast stimulus give a measure of the amount of activity produced by the adaptor. The amplitudes of these peaks are smaller in later visual areas (Figure 6) because there was only a small difference in response between the high-contrast adaptor and zero contrast test. In later visual areas, the maintained response to the adapting grating was apparently near the levels produced by the zero contrast stimulus, while in earlier areas the maintained response was at higher levels.

The weaker baseline response to the adapting grating in later visual areas was most likely due to adaptation weakening the response to the adaptor itself, rather than general unresponsiveness, since activity during the no adaptation scans was, if anything, greater in later visual areas than in early ones. By this measure of self-adaptation, then, later visual areas adapted to a much greater extent than did earlier visual areas.

Discussion

Our results have several implications for models of the cortical representation of color, summarized here and discussed further below. First, we found evidence suggesting that V1 contains large populations of both oriented and unoriented color-selective neurons. Second, responses of the unoriented neurons in V1 appeared to adapt following prolonged exposure to high-contrast stimuli. Third, our behavioral data suggest that signals from both populations contributed to the perception of color appearance. Finally, our data provide a hint that later visual areas in cortex may adapt more strongly than earlier visual areas.

Oriented and Unoriented Neurons in V1

Our results indicate that early visual cortex contains many neurons jointly selective for color and orientation. The simplest explanation of the adaptation effects observed here is that prolonged exposure to a stimulus caused neurons to reduce their responsiveness. The joint selectivity of the observed adaptation was most likely due to many of the adapted neurons being jointly selective for color and orientation. For example, adapt-

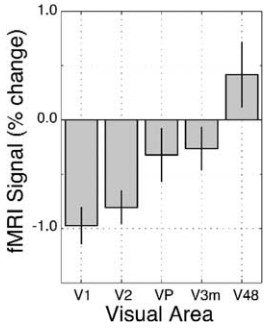

Figure 6. Amplitude of Response to the Zero Contrast Stimulus across Visual Areas

The large negative responses in early visual areas reflect the drop in response from the high levels established by the adaptor to the low level produced by the zero contrast test. Error bars plot ±one standard error of the mean. In later visual areas, the response to the adaptor was likely reduced, reflecting greater self-adaptation.

ing to a red-green horizontal pattern produced a greater reduction in response to a red-green horizontal test than to any other test. This is precisely what would be expected if adaptation reduced the responsiveness of neurons that prefer red-green horizontal patterns.

As noted above, the number of red-green neurons in V1 that are orientation selective has been widely debated (Conway, 2001; De Valois et al., 2000; Friedman et al., 2003; Johnson et al., 2001, 2004; Landisman and Ts'o, 2002a, 2002b; Lennie et al., 1990; Leventhal et al., 1995; Livingstone and Hubel, 1984; Thorell et al., 1984). Our data show that adaptation to red-green in V1 has a large component selective for both color and orientation. This finding strongly argues that V1 contains relatively large numbers of oriented red-green neurons.

We also found evidence of relatively large numbers of red-green neurons in V1 that are not tuned for orientation. Adapting to a red-green grating caused a substantial reduction in response to the orthogonal red-green pattern. The simplest explanation of these results is that some of the neurons affected by adaptation were responsive to both orientations, as are neurons with circularly symmetric receptive fields. These data represent, to our knowledge, the first neural measurements of adaptation in unoriented, red-green neurons. Our results agree with prior reports of red-green neurons with circularly symmetric receptive fields in V1 (Conway, 2001; De Valois et al., 2000; Friedman et al., 2003; Johnson et al., 2001, 2004; Landisman and Ts'o, 2002a, 2002b; Lennie et al., 1990; Leventhal et al., 1995; Livingstone and Hubel, 1984; Thorell et al., 1984) and extend them to human cortex.

The two populations of neurons appear to generate equally strong signals in V1, as indicated by the magnitude of the jointly selective and color-selective components of red-green adaptation. In most visual areas, there was a trend for larger color-selective components, which may reflect stronger signals from unoriented neurons than from oriented neurons, but these differences were not statistically reliable. The amplitudes of signals from the two populations depend upon the particular stimulus configurations used here and so may not directly reflect absolute numbers of neurons (for a detailed discussion see Schluppeck and Engel, 2002). Our conclusions regarding the relative strengths of adaptation also depend to some extent upon the appropriateness of the additive model (see above).

An alternative interpretation of our results is that they do not reflect the properties of V1 neurons themselves but rather are due to effects of adaptation earlier in the visual pathways. Contrast adaptation in the retina (Chander and Chichilnisky, 2001; Smirnakis et al., 1997) or LGN (Solomon et al., 2004) cannot explain our results, however, because the adaptation we observed was orientation selective, and neurons in the human retina and LGN lack orientation selectivity. Although we cannot rule out a subcortical source for the transfer of red-green adaptation across orientation, we think it unlikely because past measurements of parvocellular LGN failed to find effects of adaptation (Derrington and Lennie, 1984; Solomon et al., 2004).

Prior work has shown that relatively long-term adaptation to contrast produces a general reduction in neural responsiveness due to a lowering of cells' resting potentials (Carandini and Ferster, 1997; Sanchez-Vives et al., 2000). Our interpretation that the jointly selective and color-selective components of adaptation reflect oriented and unoriented neural populations is consistent with this mechanism. Adaptation also changes the tuning properties of neurons, however (e.g., Dragoi et al., 2000), though such effects may be small compared to the overall drop in responsiveness (Carandini et al., 1997). While tuning changes may underlie some of the adaptation that we observed, their presence does not affect our conclusions greatly. The color-selective red-green adaptation we observed that transferred across orientation likely originated in unoriented cells, because changes in tuning caused by adaptation are not so large as to affect responses at the orthogonal orientation. The jointly selective red-green adaptation we observed must arise in part from oriented neurons that respond to red-green; if only unoriented neurons adapted, then the effects should transfer across orientation in their entirety. The precise color tuning of the oriented neurons that give rise to the joint adaptation effects remains unknown, however. The adapted cells could prefer noncardinal directions as long as they are numerous enough to give a robust response to our red-green stimuli.

The long-term contrast adaptation studied here may also differ from effects of relatively brief prior exposures that have been studied previously (Muller et al., 1999; Boynton and Finney, 2003). Still other mechanisms may underlie the McCollough effect, which unlike traditional contrast adaptation produces positive aftereffects and transfers little between eyes (e.g., Barnes et al., 1999).

Effects of Adaptation in Extrastriate Cortex

Results in extrastriate visual areas were generally similar to those in V1, but interpreting them is complicated by uncertainty regarding the source of the adaptation effects. One possibility is that the adaptation we measured reflected a reduction in the intrinsic responsiveness of extrastriate neurons. Our data would then indicate that these areas contain large numbers of both

oriented and unoriented red-green neurons. Such an interpretation agrees with the results of prior studies that have measured both color and orientation tuning in V2, VP, or V4 using single-unit recording (Burkhalter and Van Essen, 1986; Gegenfurtner et al., 1996; Kiper et al., 1997; Levitt et al., 1994; Schein and Desimone, 1990; Shipp and Zeki, 2002).

Alternatively, adaptation effects in later visual areas could reflect changes in input from earlier visual areas, rather than adaptation of the local neurons. Under this assumption, our results no longer necessarily reveal local neural selectivity; the weakened extrastriate responses would simply reflect input from adapted orientation- and color-selective neurons in V1. Single-unit recordings suggest, for example, that under some conditions, adaptation observed in MT is mainly due to decreased input from V1 (Kohn and Movshon, 2003). Our data do not allow us to distinguish between the two possible and nonexclusive models of extrastriate adaptation.

Though they must be interpreted with care, we nevertheless observed two differences between V1 and later visual areas. First, in areas V2 and V3m, adaptation to a light-dark pattern reduced responses to red-green patterns of the same orientation, suggesting the presence of signals from oriented neurons responsive to both red-green and light-dark. We cannot definitively localize these neurons, but our data do indicate that they project relatively heavily to the dorsal stream. The fact that we saw this pattern only for light-dark adaptation is probably due to the additional presence of larger numbers of neurons tuned exclusively for light-dark. Adapting to red-green would leave these neurons unaffected, and their responses would then obscure the reduction in response of the smaller population that responds to both color directions. Some evidence for neurons that pool across color directions has been reported previously along the dorsal pathway, specifically in area MT (Dougherty et al., 1999; Seidemann et al., 1999; Wandell et al., 1999).

Later visual areas also appeared to adapt to a greater extent than did earlier visual areas. One functional explanation of adaptation is that it allows neurons to signal changes in a scene while ignoring constantly present features. Our results suggest that later visual areas are increasingly able to ignore the constant adapting stimulus. Some of this ability, however, may be due to visual attention as well as adaptation.

Attention has large effects on responses in visual cortex, but it is not likely to explain the core results observed here. We controlled attention by engaging subjects in relatively demanding tasks during both test and adaptor presentations. While such controls are not perfect, it is difficult to account for the selective pattern of effects we observed using general attentional mechanisms. For example, in order for adaptation to transfer across orientation only for red-green tests with red-green adaptors, subjects would be required to vary their attention as a joint function of test color, test orientation, and adaptor color. In addition, the differences we observed between visual areas (e.g., transfer of adaptation from light-dark to red-green in V3m but not V4/8) are difficult to account for by visual attention, which would most likely affect activity in all visual areas in the same direction. Attention may explain the stronger effects of adaptation we observed in later visual areas, however. These were not selective, applying equally to each adaptor. Subjects may simply have withdrawn attention from the adaptor, and this could have reduced neural response more in later visual areas (where attentional effects are stronger, e.g., O'Connor et al., 2002) than in earlier ones.

Human ventral stream area V4/8 has been proposed to be a critical stage in the computations that produce color perception, because it shows strong response to colored stimuli and falls close to the reported locations of lesions that in humans produce achromatopsia (for a review see Zeki, 1990). In our data, V4/8 shows red-green adaptation effects that are both jointly selective and color selective, suggesting that it receives input from both oriented and unoriented red-green neurons. These results are consistent with V4/8 playing a role in color perception but do not distinguish it from other ventral stream areas. Additionally, the presence of orientation-selective signals in this region suggest that it may also participate directly in computations that underlie perception of form (Gallant et al., 2000).

Effects of Adaptation on Color Appearance

Behavioral measures of the effect of adaptation on color appearance showed similar patterns to the fMRI data, especially those from the ventral stream. Perceptual adaptation in the contrast matching task showed a component that was selective for color and orientation, in agreement with previous work that measured either detection (Bradley et al., 1988) or the tilt aftereffect (Clifford et al., 2003; Flanagan et al., 1990). Unlike previous work, perceptual adaptation to red-green also produced a color-specific component that transferred across orientations. Both the color-selective and the jointly selective components of adaptation that we measured behaviorally were also visible in our fMRI data. The general agreement between the behavioral neural effects of adaptation suggests that the populations of neurons we measured with fMRI are likely to play an important role in the computation of color appearance.

Some prior discussions of jointly selective neurons in V1 have emphasized that their main perceptual role is to provide nonluminance input to form perception (e.g., Conway et al., 2002). Oriented red-green neurons, for example, may signal the presence and local orientation of edges between reddish and greenish surfaces.

Our results support the idea that these neurons perform an additional functional role, serving as a basis for the large influence of form on color perception (Johnson et al., 2001, 2004). For example, the color appearance of a grating depends upon its spatial frequency (Poirson and Wandell, 1993). Similarly, the work reported here demonstrated that color appearance depends upon the orientation of patterns that have been viewed in the recent past. The abundant, oriented, color-selective neurons that support these effects must be considered an integral part of the neural pathways underlying color perception.

Experimental Procedures

Subjects

Four subjects (one female, three male) with normal or corrected to normal vision participated in the experiment. Subjects all scored

within normal ranges on the Farnsworth-Munsell 100 hue test. Informed consent was received from each subject, and procedures were approved by the UCLA Office for the Protection of Research Subjects.

Stimuli

Subjects viewed two patches of sinusoidal grating while fixating on a central mark. The patches were 0.5 cyc/deg, subtended 8° of visual angle, and were centered at 6° from fixation along the horizontal meridian. The edges of the patches were smoothed by convolution with a Gaussian filter.

Stimuli were presented on a rear projection screen within the bore of the MRI scanner using an LCD projector. The projector was calibrated using a Photoresearch PR-650 spectral radiometer; independence of the red, green, and blue channels was tested, and the inverse gamma function for each channel was computed. The spectral power distribution of each channel was also measured. The Smith-Pokorny cone fundamentals (Smith and Pokorny, 1975) were used to calculate relative cone responses to our stimuli.

Four types of patterns were constructed by crossing two orientations (horizontal and vertical) with two color directions (red-green and light-dark). Patterns were oriented either horizontally or vertically. In the red-green patterns, the L and M cones were stimulated equally but in opposite directions; in reddish half cycles of the grating the L cones were more stimulated than they were by the background gray, while the M cones were less stimulated than the background. In greenish half cycles, the M cones were more stimulated, and the L cones were less stimulated. The pattern appeared reddish and greenish to our subjects, and we will refer to it as red-green for convenience, even though we made no formal measurements of color categorization. Note that this pattern does not correspond to what is traditionally termed isoluminance but rather is in the color direction that provides the strongest stimulation to classical red-green neurons. In the other color direction, the L and M cones were stimulated equally and in the same direction relative to the background. These patterns appeared to alternate between slightly purplish dark regions and slightly yellowish light regions, and we will refer to them as light-dark. Patterns in both color directions contained sinusoidal modulations of L and M cone contrast ([calculated cone response – mean calculated cone response]/mean calculated cone response). S cone contrast was zero across all patterns. The total cone contrast of the patterns was defined as the square root of the sum of the squared L and M cone contrasts.

Subjects adapted to high-contrast versions of the patterns. The total cone contrast of the red-green adapting patterns was either 0.104 or 0.076 (based on individual piloting of subjects to avoid floor and ceiling effects of adaptation), and the total cone contrast of the light-dark adapting patterns was 0.377. Test patterns were lower-contrast patterns on whose response the effects of adaptation were measured. Contrasts of tests were selected to give equal responses on the basis of prior work (Engel and Furmanski, 2001). Red-green and light-dark tests had total cone contrasts of 0.038 and 0.086, respectively. When test patterns were presented, they reversed their contrast at 1 Hz. Adaptors moved across the patch either horizontally or vertically at 8 Hz and reversed their directions at random intervals. In order to minimize eye movements, adaptor motion was in opposite directions on the two sides of fixation.

Protocol

Each subject participated in two scanning sessions and two corresponding psychophysical sessions; in one the adaptors were red-green, and in the other the adaptor was light-dark. For two subjects the adaptors were vertical, and for two they were horizontal. No differences were found between horizontal and vertical adaptors, and so results were pooled across adaptor orientation.

In each scanning session, subjects viewed all four test patterns prior to and following adaptation (Figure 1). In the no adaptation scans, the test patterns were presented for 4 s in alternation with mean, gray field presentations for 21 s. Each of the four test patterns was presented four times, yielding a total of 16 test presentations in each scan. Order of the test patterns was randomized subject to the constraint that each test pattern was to be preceded by each of the others equally often. In adaptation scans, subjects initially viewed the adapting stimulus for 1 min prior to the presentation of the first test. The rest of the scan was identical to the no adaptation scan, except that the mean field presentations were replaced with presentations of the adaptor; i.e., 4 s test patterns alternated with 21 s presentations of the adaptor. A fifth test condition was introduced in the adaptation scans. These stimuli were simple mean field presentations and were labeled “zero contrast” tests. In each scanning session, subjects participated in two no adaptation and four adaptation scans, yielding a total of eight trials per test pattern prior to adaptation and 16 trials per test following adaptation. Each session ended with a “localizer” scan that was used to identify regions of cortex that represented the portion of the visual field that contained the stimulus patches. Patches of high-contrast temporally reversing checkerboard of the same size as the grating patches alternated with gray mean field every 25 s.

During scanning, subjects performed two tasks to ensure that attention did not differ between conditions. In both adaptation and no adaptation scans, subjects monitored test presentations for 500 ms increments in the contrast of the test. Two such increments occurred during each scan (in a total of 16 test presentations). The increments occurred in only one of the two bilateral tests, and subjects were instructed to indicate as quickly and accurately as possible the occurrence and side of an increment by pressing one of two keys on an MR compatible response box. Additionally, during adaptation scans the adaptor briefly disappeared on one side of the display for 250 ms once within every 3 s interval. Again, the change was unilateral, and subjects were instructed to indicate their response as quickly and accurately as possible.

fMRI data were acquired using a BOLD contrast-weighted echo-planar pulse sequence (TE = 45; TR = 2500; FA = 80; matrix = 64 × 64; FOV = 20 cm × 20 cm; voxel size 3.125 × 3.125 × 5 mm). High-resolution conventional anatomical images were acquired coplanar to the functional data. In separate sessions, T1-weighted volumetric scans were acquired for cortical flattening.

Analysis

Visual areas were identified using reversals in phase-encoded polar angle retinotopy scans (DeYoe et al., 1996; Engel et al., 1994, 1997; Sereno et al., 1995) that were acquired in a separate session and projected onto flattened representations of the cortex. Flattened maps of cortex were generated using mrFlatMesh (Teo et al., 1997; Wandell et al., 2000). Data from the retinotopy and both adaptation scans were aligned with the T1-weighted volume scans. The identified retinotopic regions were then projected into the volume of the adaptation and no adaptation scans, where they were used as regions of interest (ROIs). Our retinotopy results did not allow us to clearly distinguish the borders of regions anterior to ventral area VP; cortex immediately anterior to VP that was active in the retinotopy scans was labeled V4/V8. Similarly, we could not fully segregate regions V3 and V3a from each other and their adjacent visual area, V7, so we averaged data across a single ROI that we label V3m.

Average fMRI responses to the test stimuli were computed for the no adaptation and adaptation scans for each ROI. Pixels were included in the analysis if they passed a criterion correlation threshold in the localizer scan (changing the criterion did not change the overall pattern of results). The fMRI time series for each pixel was converted to a percent change score by subtracting and dividing by the mean of the pixel during each scan. The average time series for each ROI was then computed and broken into segments corresponding to the 25 s following the start of each test stimulus presentation. Conditional average fMRI responses were calculated by averaging the 25 segments together for each of the four test stimulus types. Segments that contained a test stimulus contrast increment (see task, above) were excluded from the average.

Amplitudes of the average fMRI responses were estimated by fitting a convolution of a gamma function with the stimulus time course to the data from each time course segment; the peak of the best-fitting model time course was taken as an estimate of response amplitude. Mean amplitudes were calculated for each subject, ROI, and condition. Shape parameters of the gamma functions were close to those from the literature (Boynton et al., 1996), but because positive and negative BOLD responses have slightly different shapes small changes in the shape were allowed to optimize fits; parameters were set to optimize the fit of the average of the

responses in the no adaptation condition and the fit of the zero contrast test in the adaptation condition. The convolved gamma functions generally fit the main peak of the time course well, as can be seen by comparing the peaks and amplitude estimates in Figures 2 and 3.

Behavior

Perceptual effects of adaptation were measured in two separate behavioral sessions, in which subjects performed an asymmetric contrast matching task. Adaptors were presented on one side of fixation only, and following 1 min of adaptation, test and adaptors alternated with the same timing as in the MRI scans. Tests were presented bilaterally, and the subjects' task was to adjust the contrast of the test presented on the unadapted side of visual space to match the apparent contrast of the test presented at the location of the adaptor. Subjects were readapted for 1 min following each match setting, and each subject set two matches to each test pattern presented in random order. Contrast matching data were analyzed by computing a score reflecting the apparent reduction in contrast produced by adaptation. This score was the difference between the contrast of the test pattern and the contrast of the match pattern divided by the contrast of the match pattern. These scores were averaged within and then across observers.

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